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		<i>DB=USPT; PLUR=YES; OP=OR</i>	
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<input type="checkbox"/>	L2	L1 and aro	0
<input type="checkbox"/>	L3	L1 and aroa	1
<input type="checkbox"/>	L4	L1 and auxotroph\$	1
<input type="checkbox"/>	L5	salmonella.clm. and (aro or aro-a or aroa or aro-b or arod or aro-d or arob or auxotroph\$)	143
<input type="checkbox"/>	L6	salmonella.clm. and (aro or aro-a or aroa or aro-b or arod or aro-d or arob or auxotroph\$).clm.	39
<input type="checkbox"/>	L7	L6 and chlamyd\$	23
<input type="checkbox"/>	L8	L6 and chlamyd\$.clm.	3

END OF SEARCH HISTORY

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		<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L1	chlamyd\$ or trachoma\$	12575
<input type="checkbox"/>	L2	L1 and (gene near therapy)	2179
<input type="checkbox"/>	L3	L1 same (gene near therapy)	71
		<i>DB=USPT; PLUR=YES; OP=OR</i>	
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<input type="checkbox"/>	L14	L13 and (plasmid or vector or gene or cytomeg\$ or virus or viral)	1
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<input type="checkbox"/>	L15	salmonell\$ same gene same therapy	218
<input type="checkbox"/>	L16	l3 and cytomeg\$	30
<input type="checkbox"/>	L17	l3 and (cmgv or cmv)	39
<input type="checkbox"/>	L18	L17 or l16	44
<input type="checkbox"/>	L19	murdin.in. or brunham.in.	149
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<input type="checkbox"/>	L21	L20 and vector.ti,ab,clm.	104
<input type="checkbox"/>	L22	L21 and (cmv or cmgv or cytomeg\$)	55

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|--------------------------|-----|--|----|
| <input type="checkbox"/> | L23 | l22 and (salmonella or auxotroph\$ or aro or attenuat\$ or mutant\$ or mutation\$) | 53 |
| | | <i>DB=EPAB,JPAB,DWPI; PLUR=YES; OP=OR</i> | |
| <input type="checkbox"/> | L24 | 9211361 | 6 |

END OF SEARCH HISTORY

US-PAT-NO: 6811783

DOCUMENT-IDENTIFIER: US 6811783 B1

TITLE: Immunogenic compositions for protection against chlamydial infection

DATE-ISSUED: November 2, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Murdin</u> ; Andrew D.	Newmarket			CA
Dunn; Pamela L.	Mississauga			CA

US-CL-CURRENT: 424/190.1; 424/185.1, 530/350, 536/23.7

CLAIMS:

We claim:

1. An immunogenic composition, comprising: a first plasmid vector comprising: a first nucleotide sequence encoding a major outer membrane protein (MOMP) of a strain of Chlamydia pneumoniae, said first nucleotide sequence being selected from the group consisting of SEQ ID Nos: 12, 13, and 14 or encoding a MOMP having an amino acid sequence selected from the group consisting of SEQ ID Nos: 15 and 16, and a first promoter sequence operatively coupled to said first nucleotide sequence for expression of said MOMP in a host; a second plasmid vector comprising: a second nucleotide sequence encoding a 76 kDa protein of a strain of Chlamydia pneumoniae, said second nucleotide sequence being selected from the group consisting of SEQ ID Nos: 1, 2, 3 and 4, and a second promoter sequence operatively coupled to said second nucleotide sequence for expression of said 76 kDa protein in a host; and a pharmaceutically-acceptable carrier therefor.

2. The immunogenic composition of claim 1 wherein the first promoter is a cytomegalovirus promoter.

3. The immunogenic composition of claim 1 wherein said second nucleotide sequence is 76 kDa protein gene sequence encoding a protein having a molecular size of about 35 kDa and having SEQ ID No: 7.

4. The immunogenic composition of claim 1 wherein said second nucleotide sequence is 76 kDa protein gene sequence encoding a protein having a molecular size of about 60 kDa and having SEQ ID No: 8 or 9.

5. The immunogenic composition of claim 1 wherein said second promoter is a cytomegalovirus promoter.

6. The immunogenic composition of claim 1 wherein said first plasmid vector is pCAMOMP and said second plasmid vector is pCA76 kDa.

7. The immunogenic composition of claim 1 wherein said first and second vectors are present in amounts such that upon administration of the composition to the host, the protective effect of the first vector is not adversely affected by the second vector and the protective effect of the second vector is not adversely affected by the first vector.

8. The immunogenic composition of claim 1 wherein said first and second vectors are present in amounts such that an enhanced protective effect is achieved in comparison to the individual vectors alone.

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-
- ☐ 1. [20050095254](#). 15 Oct 04. 05 May 05. DNA immunization against Chlamydia infection. Brunham, Robert C.. 424/190.1; 514/44 A61K048/00 A61K039/02 A61K039/118.
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- ☐ 2. [20050069942](#). 01 Nov 04. 31 Mar 05. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 435/6; 435/252.3 435/320.1 435/69.3 530/350 536/23.7 C12Q001/68 C07H021/04 C07K014/295 C12N015/74.
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- ☐ 3. [20050065106](#). 10 Sep 04. 24 Mar 05. Immunogenic compositions for protection against Chlamydial infection. Murdin, Andrew D., et al. 514/44; A61K048/00.
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- ☐ 4. [20050002960](#). 23 Jul 04. 06 Jan 05. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 424/192.1; 435/320.1 435/325 435/69.1 530/324 536/23.5 A61K039/00 C07H021/04 C07K014/47.
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- ☐ 5. [20050002944](#). 29 Dec 03. 06 Jan 05. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 424/184.1; A61K039/00 A61K039/38.
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- ☐ 6. [20040254130](#). 10 Apr 03. 16 Dec 04. Chlamydia antigens and corresponding dna fragments and uses thereof. Murdin, Andrew D., et al. 514/44; A61K048/00.
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- ☐ 10. [20040086525](#). 30 Jun 03. 06 May 04. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 424/190.1; 435/252.3 435/320.1 435/69.3 530/350 536/23.7 C07H021/04 A61K039/02 C12N001/21 C07K014/295.
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- ☐ 13. [20030224004](#). 06 Feb 03. 04 Dec 03. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 424/184.1; A61K039/00 A61K039/38.
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- ☐ 14. 20030206921. 07 Jan 03. 06 Nov 03. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 424/190.1; 435/252.3 435/320.1 435/6 435/69.3 530/350 530/388.4 536/23.7 C12Q001/68 C07H021/04 A61K039/02 C12N001/21 C07K014/295 C07K016/12.
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- ☐ 15. 20030170259. 27 Oct 99. 11 Sep 03. CHLAMYDIA ANTIGENS AND CORRESPONDING DNA FRAGMENTS AND USES THEREOF. MURDIN, ANDREW D., et al. 424/190.1; A61K039/02.
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- ☐ 16. 20030161833. 31 Dec 02. 28 Aug 03. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 424/184.1; 536/23.1 C07H021/02 C07H021/04 A61K039/00 A61K039/38.
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- ☐ 17. 20030157124. 20 Dec 02. 21 Aug 03. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 424/190.1; 435/252.3 435/320.1 435/69.3 530/350 536/23.7 A61K039/02 C07H021/04 C07K014/295 C12P021/02 C12N001/21 C12N015/74.
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☐ 31. 20020094340. 01 Dec 99. 18 Jul 02. CHLAMYDIA ANTIGENS AND CORRESPONDING DNA THEREOF. MURDIN, ANDREW D., et al. 424/263.1; A61K039/118.

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☐ 33. 20020082402. 03 Apr 01. 27 Jun 02. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 536/23.1; 424/184.1 530/350 C07H021/02 C07H021/04 A61K039/00 A61K039/38 C07K001/00 C07K014/00 C07K017/00.

☐ 34. 20020081682. 28 Jun 01. 27 Jun 02. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 435/183; 424/263.1 435/252.3 435/320.1 435/69.3 536/23.7 C12N009/00 C07H021/04 A61K039/118 C12N001/21 C12P021/02 C12N015/74.

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☐ 36. 20020037293. 22 Jun 01. 28 Mar 02. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin, Andrew D., et al. 424/190.1; 424/263.1 435/252.3 435/320.1 435/69.3 536/23.7 A61K039/118 C07H021/04 C12N001/21 C12P021/02 C12N015/74.

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☐ 39. 6811783. 07 Sep 99; 02 Nov 04. Immunogenic compositions for protection against chlamydial infection. Murdin; Andrew D., et al. 424/190.1; 424/185.1 530/350 536/23.7. A61K039/02 A61K039/00 C07K001/00 C07H021/04 .

☐ 40. 6808713. 16 Oct 01; 26 Oct 04. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin; Andrew D., et al. 424/263.1; 424/178.1 424/184.1 424/190.1 424/200.1 435/252.3 435/254.11 435/320.1 435/69.1 435/69.3 435/70.1 530/350 536/23.1 536/23.7. A61K039/118 A61K039/02 C12N001/20 C12P021/04 C07H021/04 .

☐ 41. 6696421. 12 Aug 99; 24 Feb 04. DNA immunization against chlamydia infection. Brunham; Robert C.. 514/44; 424/184.1 424/263.1 435/320.1 435/69.1. A61K048/00 A61K039/00 A61K039/118 C12N015/63 C12N015/00 .

☐ 42. 6693087. 20 Aug 99; 17 Feb 04. Nucleic acid molecules encoding POMP91A protein of Chlamydia. Murdin; Andrew D., et al. 514/44; 424/130.1 536/23.4. A61K039/395 A61K031/70 C07H021/04 .

☐ 43. 6686339. 15 Jun 01; 03 Feb 04. Nucleic acid molecules encoding inclusion membrane protein C of Chlamydia. Murdin; Andrew D., et al. 514/44; 424/93.2 435/320.1 536/23.1 536/23.2 536/24.1. A61K048/00 A61K035/66 C12N015/63 C07H021/04 .

☐ 44. 6676949. 03 Dec 99; 13 Jan 04. Two-step immunization procedure against Chlamydia infection. Brunham; Robert C., et al. 424/263.1; 424/200.1 424/93.1 435/252.1 435/320.1 435/325 435/419 435/455 435/468 435/471 435/7.36 530/350 536/23.2 536/23.5 536/23.7 536/24.1 536/24.31 800/278 800/295 800/298. C12N015/31 .

☐ 45. 6660275. 26 Jul 99; 09 Dec 03. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin; Andrew D., et al. 424/263.1; 424/184.1 424/185.1 424/190.1 435/7.36 435/89 435/91.1 435/91.31 435/91.4 435/91.42. A61K039/00 A61K039/38 A61K039/02 A61K039/118 G01N038/571 .

☐ 46. 6649370. 26 Oct 99; 18 Nov 03. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin; Andrew D., et al. 435/69.1; 435/252.3 435/320.1 435/325 536/23.7. C12P021/06 C12N001/20 C12N015/00 C12N005/00 C07H021/04 .

☐ 47. 6642025. 13 Jul 01; 04 Nov 03. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin; Andrew D., et al. 435/69.1; 435/320.1 435/69.3 435/69.7 435/69.8 435/71.1 435/71.2 536/23.1 536/23.7 536/24.1 536/24.2 536/24.32. C12P021/06 .

☐ 48. 6632663. 22 Sep 99; 14 Oct 03. DNA immunization against chlamydia infection. Brunham; Robert C.. 435/320.1; C12N015/63 .

☐ 49. 6607730. 29 Oct 99; 19 Aug 03. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin; Andrew D., et al. 424/263.1; 424/184.1 424/185.1 424/190.1 424/200.1 424/234.1 424/278.1 435/7.36 530/389.5. A61K039/00 A61K039/38 A61K039/02 A61K039/118 A61K047/00 .

☐ 50. 6403102. 27 Oct 99; 11 Jun 02. Chlamydia antigens and corresponding DNA fragments and uses thereof. Murdin; Andrew D., et al. 424/263.1; 424/185.1 424/190.1 424/192.1 530/350. A61K039/118 .

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Term	Documents
CMV	27399
CMVS	45
CMGV	2
CMGVS	0

CYTOMEG\$	0
CYTOMEG	3
CYTOMEGA	14
CYTOMEGABOVIRUS	3
CYTOMEGAGALOVIRUS	1
CYTOMEGAHOVIRUS	1
CYTOMEGAIOVIRUS	7
(L21 AND (CMV OR CMGV OR CYTOMEG\$)).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	55

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File: DWPI

Oct 5, 2005

DERWENT-ACC-NO: 2003-441771

DERWENT-WEEK: 200565

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TITLE: New DNA and proteins comprising a portion of a Chlamydia antigen, useful for diagnosing or treating Chlamydial infections, particularly as vaccines for treating or preventing Chlamydial infections, e.g. pelvic inflammatory disease

INVENTOR: BARTH, B; BHATIA, A ; GUDERIAN, J ; MAISONNEUVE, J L ; PROBST, P ; SKEIKY, Y A W

PATENT-ASSIGNEE: CORIXA CORP (CORIN)

PRIORITY-DATA: 2002US-0197220 (July 15, 2002), 2001US-0012256 (November 6, 2001), 2001US-0007693 (December 5, 2001), 2000US-198853P (April 21, 2000), 2000US-219752P (July 20, 2000), 2001US-0841260 (April 23, 2001)

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PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<input type="checkbox"/> EP 1581092 A2	October 5, 2005	E	000	A61B001/00
<input type="checkbox"/> WO 2003041560 A2	May 22, 2003	E	275	A61B000/00
<input type="checkbox"/> AU 2002363638 A1	May 26, 2003		000	A61B000/00
<input type="checkbox"/> US 20050084499 A1	April 21, 2005		000	C07K014/295
<input type="checkbox"/> US 6919187 B2	July 19, 2005		000	C12P021/06

DESIGNATED-STATES: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LU MC NL PT SE SK TR AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
EP 1581092A2	November 5, 2002	2002EP-0799875	
EP 1581092A2	November 5, 2002	2002WO-US35624	
EP 1581092A2		WO2003041560	Based on
WO2003041560A2	November 5, 2002	2002WO-US35624	
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US20050084499A1	April 21, 2000	2000US-198853P	Provisional
US20050084499A1	July 20, 2000	2000US-219752P	Provisional

US20050084499A1	April 23, 2001	2001US-0841260	CIP of
US20050084499A1	November 6, 2001	2001US-0012256	CIP of
US20050084499A1	December 5, 2001	2001US-0007693	CIP of
US20050084499A1	July 15, 2002	2002US-0197220	
US 6919187B2	July 15, 2002	2002US-0197220	

INT-CL (IPC): A61 B 0/00; A61 B 1/00; A61 K 31/118; A61 K 39/02; C07 H 21/04;
C07 K 14/295; C12 P 21/06

RELATED-ACC-NO: 2001-616771

ABSTRACTED-PUB-NO: WO2003041560A

BASIC-ABSTRACT:

NOVELTY - A new isolated polynucleotide has a sequence comprising:

- (a) any of 26 DNA sequences with 732-4257 base pairs (bp) fully defined in the specification;
- (b) the complements of (a);
- (c) at least 20 contiguous residues of (a);
- (d) a sequence that hybridizes to (a) under highly stringent conditions;
- (e) sequences having at least 95-99% identity to (a); or
- (f) degenerate variants of (a).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polypeptide comprising an amino acid sequence encoded by the new polynucleotide above, or having at least 95-99% identity to the encoded amino acid sequence; or comprising at least an immunogenic fragment of a polypeptide sequence:

(a) comprising any of 9 sequences having 542-1419 amino acids fully defined in the specification;

(b) having at least 95-99% identity with (1.a); or

(c) consisting of at least 10 contiguous residues of (1.a);

(2) an expression vector comprising the polynucleotide operably linked to an expression control sequence;

(3) a host cell transformed or transfected with the expression vector;

(4) an isolated antibody, or its antigen-binding fragment, which specifically binds to the polypeptide above;

(5) a method for detecting or determining the presence of Chlamydia;

(6) a fusion protein comprising at least one of the polypeptide cited above;

(7) an oligonucleotide that hybridizes to any of the 26 DNA sequences cited above, under highly stringent conditions;

(8) a method for stimulating and/or expanding T cells specific for a Chlamydia protein;

(9) an isolated T cell population comprising T cells prepared in method (8);

(10) a composition comprising a first component consisting of physiological carriers and immunostimulants, and a second component consisting of:

(a) the polypeptide cited above;

(b) the polynucleotide cited above;

(c) the antibody of (4);

(d) the fusion protein of (6);

(e) the T cell population of (9); or

(f) an antigen-presenting cell that expresses the polypeptide cited above;

(11) a method for stimulating an immune response in a patient;

(12) methods for the treatment of Chlamydia infection in a patient; and

(13) diagnostic kits comprising:

(a) at least one oligonucleotide cited in (7); or

(b) at least one antibody cited in (4), and a detection reagent, where the detection reagent comprising a reporter group.

ACTIVITY - Antibiotic; Antiinflammatory; Antiinfertility; Cardiant; Antiarteriosclerotic; Ophthalmological.

MECHANISM OF ACTION - Gene Therapy; Vaccine. A murine model of genital tract infection with human serovar K strain of *C. trachomatis* (Ct), which closely resembled the pathology of infection in humans, was employed. Balb/c mice were vaccinated with a formulation comprising SBAS1 and 10 micro g of a recombinant form of major outer membrane protein (MOMP) from serovar F, pmpC from serovar L2, or pmpG from serovar L2. Control animals consisted of 2 uninfected animals, 2 AS1-sham vaccinated /infected animals, and 2 animals immunized with AS1-adjuvant and UV-irradiated EB. Four weeks following the final vaccination, the animals were treated with 1.25 mg of progesterone prior to being infected with 1 multiply 10⁷ IFU of purified serovar K. Results showed that mice vaccinated with MOMP, pmpG and pmpC demonstrated reduced bacterial shedding 4 days post-infection when compared to controls. These showed heterotypic protection against Ct genital infection.

USE - The polynucleotide, polypeptide, compositions or methods are useful for the serodiagnosis or treatment of Chlamydial infections, particularly in humans. The polynucleotide, polypeptide or compositions are particularly useful for stimulating an immune response in a patient, or for stimulating and/or expanding T cells specific for a Chlamydia protein (all claimed). Specifically, the polynucleotide,

polypeptide or compositions are useful as vaccines for treating or preventing Chlamydial infections including pelvic inflammatory disease (which results in tubal obstruction and infertility in women), male infertility, ocular infection (which may cause blindness), acute respiratory tract infections, atherosclerosis, or coronary heart disease.

ABSTRACTED-PUB-NO: WO2003041560A
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/0

DERWENT-CLASS: B04 D15 D16 P31

CPI-CODES: B04-B03C; B04-C01G; B04-E03F; B04-E05; B04-E08; B04-F01; B04-F0100E; B04-F10A; B04-G01; B04-N04A; B04-N08; B11-C07A; B11-C08E; B11-C08E5; B12-K04A4; B12-K04F; B14-A01A; B14-C03; B14-F01; B14-F07; B14-G01; B14-K01; B14-P02; B14-S03A; B14-S11B; D05-H04; D05-H07; D05-H08; D05-H09; D05-H11; D05-H12A; D05-H12D1; D05-H12E; D05-H18;

DOCUMENT-IDENTIFIER: US 6693087 B1

TITLE: Nucleic acid molecules encoding POMP91A protein of Chlamydia

Detailed Description Text (134):

REFERENCES 1. Grayston et al. (1995) Journal of Infectious Diseases 168:1231. 2. Campos et al. (1995) Investigation of Ophthalmology and Visual Science 36:1477. 3. Grayston et al (1990) Journal of Infectious Diseases 161:618. 4. Marrie (1993) Clinical Infectious Diseases. 18:501. 5. Wang et al (1986) Chlamydial infections. Cambridge University Press, Cambridge.p. 329. 6. Norman et al., Acta Paediatrica, 1998, Vol 87, Iss 1, pp 23-27. 7. Saikku et al.(1988) Lancet;ii:983. 8. Thom et al. (1992) JAMA 268:68. 9. Linnanmaki et al. (1993), Circulation 87:1030. 10. Saikku et al. (1992)Annals Internal Medicine 116:273. 11. Melnick et al(1993) American Journal of Medicine 95:499. 12. Shor et al. (1992) South African. Medical Journal 82:158. 13. Kuo et al. (1993) Journal of Infectious Diseases 167:841. 14. Kuo et al. (1993) Arteriosclerosis and Thrombosis 13:1500. 15. Campbell et al (1995) Journal of Infectious Diseases 172:585. 16. Chiu et al. Circulation, 1997 (In Press). 17. Ramirez et al (1996) Annals of Internal Medicine 125:979. 18. Jackson et al. Abst. K121, p272, 36th ICAAC, Sep. 15-18 , 1996, New Orleans. 19. Fong et al (1997) Journal of Clinical Microbiology 35:48. 20. Hahn D L, et al. Evidence for Chlamydia pneumoniae infection in steroid-dependent asthma. Ann Allergy Asthma Immunol. 1998 January; 80(1): 45-49. 21. Hahn D L, et al. Association of Chlamydia pneumoniae IgA antibodies with recently symptomatic asthma. Epidemiol Infect. 1996 December; 117(3): 513-517. 22. Bjornsson E, et al. Serology of chlamydia in relation to asthma and bronchial hyperresponsiveness. Scand J Infect Dis. 1996; 28(1): 63-69. 23. Hahn D L. Treatment of Chlamydia pneumoniae infection in adult asthma: a before-after trial. J Fam Pract. 1995 October; 41(4): 345-351. 24. Allegra L, et al. Acute exacerbations of asthma in adults: role of Chlamydia pneumoniae infection. Eur Respir J. 1994 December; 7(12): 2165-2168. 25. Hahn D L, et al. Association of Chlamydia pneumoniae (strain TWAR) infection with wheezing, asthmatic bronchitis, and adult-onset asthma. JAMA. July 10, 1991; 266(2): 225-230. 26. Pal et al.(1996) Infection and Immunity.64:5341. 27. Jones et al. (1995) Vaccine 13:715. 28. Igietsemes et al. (1993) Immunology 5:317. 29. Igietseme et al (1993) Regional Immunology 5:317. 30. Magee et al (1993) Regional Immunology 5:305. 31. Landers et al (1991) Infection & Immunity 59:3774. 32. Magee et al (1995) Infection & Immunity 63:516. 33. Cotter et al. (1995) Infection and Immunity 63:4704. 34. Campbell et al (1990) Infection and Immunity 58:93. 35. McCafferty et al (1995) Infection and Immunity 63:2387-9. 36. Knudsen et al (1996) Third Meeting of the European Society for Chlamydia Research, Vienna. 37. Wiedmann-Al-Ahmad M, et al. Reactions of polyclonal neutralizing anti-p54 monoclonal antibodies with an isolated, species-specific 54-kilodalton protein of Chlamydia pneumoniae. Clin Diagn Lab Immunol. 1997 November; 4(6): 700-704. 38. Hughes et al., 1992. Infect. Immun. 60(9):3497. 39. Dion et al., 1990. Virology 179:474-477. 40. Snijders et al., 1991. J. Gen. Virol. 72:557-565. 41. Langeveld et al., Vaccine 12(15):1473-1480, 1994. 42. Ausubel et al., Current Protocols in Molecular Biology, John Wiley & Sons Inc., 1994. 43. Kunkel et al. Proc. Natl. Acad. Sci. USA (1985) 82:448. 44. Silhavy et al. Experiments with Gene Fusions, Cold Spring Harbor Laboratory press, 1984. 45. Davis et al. A Manual for Genetic Engineering: Advanced Bacterial Genetics, Cold Spring Harbor Laboratory Press, 1980). 46. Casey & Davidson, Nucl. Acid Res. (1977) 4:1539. 47. Cagnon et al., Protein Engineering (1991) 4(7):843. 48. Takase et al., J. Bact. (1987) 169:5692. 49. Perez Melgosa et al., Infect Immun (1994) 62:880. 50. Watson et al., Nucleic Acids Res (1990) 18:5299. 51. Watson et al., Microbiology (1995) 141:2489. 52. Melgosa et al., FEMS Microbiol Lett (1993) 112:199. 53. Campbell et al., J Clin Microbiol (1990) 28:1261. 54. Iijima et al., J Clin Microbiol (1994) 32:583. 54. Tartaglia et al, Virology (1992) 188:217. 55. Taylor et al, Vaccine (1995) 15:359. 56. Kieny et al., Nature (1994) 312:163. 57. Mekalanos et al., Nature (1983) 306:551. 58. Nakayama et al., Bio/Tech. (1988) 6:693. 59. High et al., EMBO (1992) 11:1991. 60. Sizemore et al., Science (1995) 270:299. 61. Medaglini et al., Pro. Natl. Acad. Sci. USA (1995) 92:6868. 62. Flynn J. L., Cell. Mol. Biol. (1994) 40 (suppl. I):31. 63. Norton & Coffin, Molec. Cell Biol. (1985) 5:281. 64. Li et al., Gene (1989) 78:243. 65. Li & Paulin, J. Biol. Chem. (1991) 266:6562. 66. Li & Paulin, J. Biol.

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Chem. (1993) 268:10403. 67. Hartikka et al., Human Gene Therapy (1996) 7:1205. 68. Tang et al., Nature (1992) 356:152. 69. Furth et al., Vaccine 1994, 12:1503-1509. 70. Nielsen et al., Science (1991) 254:1497. 71. Southern, J. Mol. Biol. (1975) 98:503. 72. Dunn et al., Cell (1977) 12:23. 73. Towbin et al., Proc. Natl. Acad. Sci. USA (1979) 76:4350. 74. Laemmli, Nature (1970) 227:680. 75. Bachmaier et al., Science (1999) 283:1335. 76. Yang et al., 1993, Infection & Immunity, vol. 61, pp 2037-40. 77. Chi E. Y., Kuo C. C., Grayston J. T., 1987. Unique ultrastructure in the elementary body of Chlamydia sp strain TWAR. J. Bacteriol 169(8):3757-63. 78. Needleman, S. B., and Wunsch, C. D. 1970, J. Mol Biol. 48:443-453. 79. Sellers, P. H. 1974 On the theory and computation of evolutionary distances. J. Appl. Math(Siam) 26:787-793. 80. Waterman, M. S., Smith, T. F., and Beyer, W. A. 1976. Advan. Math. 20:367-387. 81. Smith, T. F., and Waterman, M. S. 1981 Identification of common molecular subsequences. J. Mol. Biol. 147:195-197. 82. Sobel, E. and Martinez, H. M. 1985 A Multiple Sequence Alignment Program. Nucleic Acid Res. 14:363-374.

DOCUMENT-IDENTIFIER: US 6565856 B1

TITLE: Compounds and methods for treatment and diagnosis of chlamydial infection

Detailed Description Text (35):

A genomic library of Chlamydia trachomatis LGV II was constructed by limited digests using BamHI, BglII, BstYI and MboI restriction enzymes. The restriction digest fragments were subsequently ligated into the BamHI site of the retroviral vectors pBIB-KS1,2,3. This vector set was modified to contain a Kosak translation initiation site and stop codons in order to allow expression of proteins from short DNA genomic fragments, as shown in FIG. 2. DNA pools of 80 clones were prepared and transfected into the retroviral packaging line Phoenix-Ampho, as described in Pear, W. S., Scott, M. L. and Nolan, G. P., Generation of High Titre, Helper-free Retroviruses by Transient Transfection. Methods in Molecular Medicine: Gene Therapy Protocols, Humana Press, Totowa, N.J., pp. 41-57. The Chlamydia library in retroviral form was then transduced into H2-Ld expressing P815 cells, which were then used as target cells to stimulate an antigen specific T-cell line.

DOCUMENT-IDENTIFIER: US 6555115 B1

**** See image for Certificate of Correction ****

TITLE: Compounds and methods for treatment and diagnosis of chlamydial infection

Detailed Description Text (97):

A genomic library of Chlamydia trachomatis LGV II was constructed by limited digests using BamHI, BglII, BstYI and MboI restriction enzymes. The restriction digest fragments were subsequently ligated into the BamHI site of the retroviral vectors pBIB-KS1,2,3. This vector set was modified to contain a Kosak translation initiation site and stop codons in order to allow expression of proteins from short DNA genomic fragments, as shown in FIG. 2. DNA pools of 80 clones were prepared and transfected into the retroviral packaging line Phoenix-Ampho, as described in Pear, W. S., Scott, M. L. and Nolan, G. P., Generation of High Titre, Helper-free Retroviruses by Transient Transfection. Methods in Molecular Medicine: Gene Therapy Protocols, Humana Press, Totowa, N.J., pp. 41-57. The Chlamydia library in retroviral form was then transduced into H2-Ld expressing P815 cells, which were then used as target cells to stimulate an antigen specific T-cell line.

DOCUMENT-IDENTIFIER: US 6448234 B1

TITLE: Compounds and methods for treatment and diagnosis of chlamydial infection

Detailed Description Text (158):

A genomic library of *Chlamydia trachomatis* LGV II was constructed by limited digests using BamHI, BglII, BstYI and MboI restriction enzymes. The restriction digest fragments were subsequently ligated into the BamHI site of the retroviral vectors pBIB-KS1,2,3. This vector set was modified to contain a Kosak translation initiation site and stop codons in order to allow expression of proteins from short DNA genomic fragments, as shown in FIG. 2. DNA pools of 80 clones were prepared and transfected into the retroviral packaging line Phoenix-Ampho, as described in Pear, W. S., Scott, M. L. and Nolan, G. P., Generation of High Titre, Helper-free Retroviruses by Transient Transfection. Methods in Molecular Medicine: Gene Therapy Protocols, Humana Press, Totowa, N.J., pp. 41-57. The *Chlamydia* library in retroviral form was then transduced into H2-Ld expressing P815 cells, which were then used as target cells to stimulate an antigen specific T-cell line.

DOCUMENT-IDENTIFIER: US 5648251 A

TITLE: Method of transduction of cells with retroviral vectors

Detailed Description Text (51):

An efficient transduction method is a key component for clinical utilization in clinical trials. Most protocols incorporate a 37.degree. C. incubation tempature for various transduction times. A novel transduction procedure has been developed using the combination of centrifugation and 32.degree. C. overnight incubation. Centrifugation has been used for improved detection of other viruses, and chlamydia in clinical specimens (Ripa and Mardh Nongonococcal Urethritis and Related Infections, Holmes, et al., eds., American Society for Microbiology, Washington, D.C., pgs. 323-327, 1977; Heggie and Huang, J. Virol. Methods, Vol 41, pgs. 1-7, 1993) The combination of centrifugation and overnight transduction of NIH-3T3 TK.sup.- cells at 32.degree. C. resulted in a 4- to 18-fold increase compared to the overnight transduction at 32.degree. C. The actual mechanism for the success of this centrifugation method is not well understood; however, aggregation of vector particles and/or vector particles with debris may play a role. The supernatants from roller bottles and cCellCube appeared to be more viscous than supernatant from the 175 flask, although all supernatants were filtered through a 1.2 .mu.m filter. Transduction by centrifugation on human leukemic HUT 78 cells also demonstrated a significant increase in trasnduction efficiency as determined by FACS and PCR analysis. This technique may result in a dramatic impact for successful gene therapy, especially where vector is in limited concentration. Studies of transduction on clinically relevant target cells such as peripheral blood lymphocytes (PBL), tumor infiltrating lymphocytes (TIL), bone marrow cells, and tumor cells are in progress.

Salmonella (R. Powell et al., In: Molecular Approaches to the control of infectious diseases, pp. 183-187, F. Bran, E. Norrby, D. Burton, and J. Meckalanos (eds), Cold Spring Harbor Press, Cold Spring Harbor, N.Y. (1996);

DOCUMENT-IDENTIFIER: US 20050221445 A1

TITLE: Virus coat protein/receptor chimeras and methods of use

Detail Description Paragraph:

[0097] Mammalian expression systems further include vectors specifically designed for "gene therapy" methods, including adenoviral vectors (U.S. Pat. Nos. 5,700,470 and 5,731,172), adeno-associated vectors (U.S. Pat. No. 5,604,090), herpes simplex virus vectors (U.S. Pat. No. 5,501,979), and retroviral vectors (U.S. Pat. Nos. 5,624,820, 5,693,508 and 5,674,703 and WIPO publications WO92/05266 and WO92/14829). The chimeric polypeptide encoding gene can be introduced into vaccine delivery vehicles, such as attenuated vaccinia (M. Girard et al., C R Acad Sci III., 322:959-66 (1999); B. Moss et al., AIDS, 2 Suppl 1:S103-5 (1988)), Semiliki-forest virus (M. Girard et al., C R Acad Sci III., 322:959-66 (1999); S. P. Mossman et al., J Virol., 70: 19.53-60 (1996)), or Salmonella (R. Powell et al., In: Molecular Approaches to the control of infectious diseases, pp. 183-1 87, F. Bran, E. Norrby, D. Burton, and J. Meckalanos (eds), Cold Spring Harbor Press, Cold Spring Harbor, N.Y. (1996); M. T. Shata et al., Mol Med Today, 6:66-71 (2000)) to provide an efficient and reliable means for the expression of properly associated and folded virus coat protein and receptor sequences, for example, gp120 and CD4.

DOCUMENT-IDENTIFIER: US 20040219169 A1

TITLE: Compositions and methods for delivery of an agent using attenuated Salmonella containing phage

Detail Description Paragraph:

[0112] Cytokine immunotherapy is a modification of immunogene therapy and involves the administration of tumor cell vaccines that are genetically modified ex vivo or in vivo to express various cytokine genes. In animal tumor models, cytokine gene transfer resulted in significant antitumor immune response (Fearon, et al., 1990, Cell 60:387-403; Wantanabe, et al., 1989, Proc. Nat. Acad. Sci. USA, 86:9456-9460). Thus, in the present invention, the Salmonella containing phage are used to deliver nucleic acid molecules that encode a cytokine, such as IL-1, IL-2, IL-4, IL-5, IL-15, IL-18, IL-12, IL-10, GM-CSF, INF-.gamma., INF-.alpha., SLC, endothelial monocyte activating protein-2 (EMAP2), MIP-3.alpha., MIP-3.beta., or an MHC gene, such as HLA-B7. Additionally, other exemplary cytokines include members of the TNF family, including but not limited to tumor necrosis factor-.alpha. (TNF-.alpha.), tumor necrosis factor-.beta. (TNF-.beta.), TNF-.alpha.-related apoptosis-inducing ligand (TRAIL), TNF-.alpha.-related activation-induced cytokine (TRANCE), TNF-.alpha.-related weak inducer of apoptosis (TWEAK), CD40 ligand (CD40L), LT-.alpha., LT-.beta., OX40L, CD40L, FasL, CD27L, CD30L, 4-1BBL, APRIL, LIGHT, TL1, TNFSF16, TNFSF17, and AITR-L, or a functional portion thereof See, e.g., Kwon et al., 1999, Curr. Opin. Immunol. 11:340-345 for a general review of the TNF family. Delivery of these gene products will modulate the immune system, increasing the potential for host antitumor immunity. Alternatively, nucleic acid molecules encoding costimulatory molecules, such as B7.1 and B7.2, ligands for CD28 and CTLA-4 respectively, can also be delivered to enhance T cell mediated immunity. These gene products can be co-delivered with cytokines, using the same or different promoters and optionally with an internal ribosome binding site. Similarly, .alpha.-1,3-galactosyl transferase expression on tumor cells allows complement-mediated cell killing.

DOCUMENT-IDENTIFIER: US 20040234536 A1

TITLE: Compounds and methods for treatment and diagnosis of chlamydial infection

Detail Description Paragraph:

[0691] Excellent murine leukemia virus (MLV)-based viral expression vectors have been developed by Kim et al. (1998). In creating the MLV vectors, Kim et al. found that the entire gag sequence, together with the immediate upstream region, could be deleted without significantly affecting viral packaging or gene expression. Further, it was found that nearly the entire U3 region could be replaced with the immediately-early promoter of human cytomegalovirus without deleterious effects. Additionally, MCR and internal ribosome entry sites (IRES) could be added without adverse effects. Based on their observations, Kim et al. have designed a series of MLV-based expression vectors comprising one or more of the features described above.

Detail Description Paragraph:

[0775] A genomic library of Chlamydia trachomatis LGV II was constructed by limited digests using BamHI, BglII, BstYI and MboI restriction enzymes. The restriction digest fragments were subsequently ligated into the BamHI site of the retroviral vectors pBIB-KS1,2,3. This vector set was modified to contain a Kosak translation initiation site and stop codons in order to allow expression of proteins from short DNA genomic fragments, as shown in FIG. 2. DNA pools of 80 clones were prepared and transfected into the retroviral packaging line Phoenix-Ampho, as described in Pear, W. S., Scott, M. L. and Nolan, G.P., Generation of High Titre, Helper-free Retroviruses by Transient Transfection. Methods in Molecular Medicine: Gene Therapy Protocols, Humana Press, Totowa, N.J., pp. 41-57. The Chlamydia library in retroviral form was then transduced into H2-Ld expressing P815 cells, which were then used as target cells to stimulate an antigen specific T-cell line.

DOCUMENT-IDENTIFIER: US 20040204345 A1

TITLE: Modulation of endogenous gene expression in cells

Detail Description Paragraph:

[0164] Furthermore, the product of the human cytomegalovirus (HCMV) UL34 open reading frame acts as a transcriptional repressor of certain HCMV genes, for example, the US3 gene. LaPierre et al. (2001) J. Virol. 75:6062-6069. Accordingly, the UL34 gene product, or functional fragments thereof, can be used as a component of a fusion polypeptide also comprising a zinc finger binding domain. Nucleic acids encoding such fusions are also useful in the methods and compositions disclosed herein.

Detail Description Paragraph:

[0168] Additional exemplary repression domains include those derived from histone deacetylases (HDACs, e.g., Class I HDACs, Class II HDACs, SIR-2 homologues), HDAC-interacting proteins (e.g., SIN3, SAP30, SAP15, NCoR, SMRT, RB, p107, p130, RBAP46/48, MTA, Mi-2, Brg1, Brm), DNA-cytosine methyltransferases (e.g., Dnmt1, Dnmt3a, Dnmt3b), proteins that bind methylated DNA (e.g., MBD1, MBD2, MBD3, MBD4, MeCP2, DMAP1), protein methyltransferases (e.g., lysine and arginine methylases, SuVar homologues such as Suv39H1), polycomb-type repressors (e.g., Bmi-1, eed1, RING1, RYBP, E2F6, Mel18, YY1 and CtBP), viral repressors (e.g., adenovirus Elb 55K protein, cytomegalovirus UL34 protein, viral oncogenes such as v-erbA), hormone receptors (e.g., Dax-1, estrogen receptor, thyroid hormone receptor), and repression domains associated with naturally-occurring zinc finger proteins (e.g., WT1, KAP1). Further exemplary repression domains include members of the polycomb complex and their homologues, HPH 1, HPH2, HPC2, NC2, groucho, Eve, tramtrak, mHP1, SIP1, ZEB1, ZEB2, and Enx1/Ezh2. In all of these cases, either the full-length protein or a functional fragment can be used as a repression domain for fusion to a zinc finger binding domain. Furthermore, any homologues of the aforementioned proteins can also be used as repression domains, as can proteins (or their functional fragments) that interact with any of the aforementioned proteins.

Detail Description Paragraph:

[0252] ZFPs and expression vectors encoding ZFPs can be administered directly to the patient for modulation of gene expression and for therapeutic or prophylactic applications, for example, cancer, ischemia, diabetic retinopathy, macular degeneration, rheumatoid arthritis, psoriasis, HIV infection, sickle cell anemia, Alzheimer's disease, muscular dystrophy, neurodegenerative diseases, vascular disease, cystic fibrosis, stroke, and the like. Examples of microorganisms that can be inhibited by ZFP gene therapy include pathogenic bacteria, e.g., chlamydia, rickettsial bacteria, mycobacteria, staphylococci, streptococci, pneumococci, meningococci and conococci, klebsiella, proteus, serratia, pseudomonas, legionella, diphtheria, salmonella, bacilli, cholera, tetanus, botulism, anthrax, plague, leptospirosis, and Lyme disease bacteria; infectious fungus, e.g., Aspergillus, Candida species; protozoa such as sporozoa (e.g., Plasmodia), rhizopods (e.g., Entamoeba) and flagellates (Trypanosoma, Leishmania, Trichomonas, Giardia, etc.); viral diseases, e.g., hepatitis (A, B, or C), herpes virus (e.g., VZV, HSV-1, HSV-6, HSV-II, CMV, and EBV), HIV, Ebola, adenovirus, influenza virus, flaviviruses, echovirus, rhinovirus, coxsackie virus, comovirus, respiratory syncytial virus, mumps virus, rotavirus, measles virus, rubella virus, parvovirus, vaccinia virus, HTLV virus, dengue virus, papillomavirus, poliovirus, rabies virus, and arboviral encephalitis virus, etc.

Detail Description Paragraph:

[0316] Three expression vectors were constructed for these studies. The general design is summarized in FIG. 5. The vectors are derived from pcDNA3.1 (+) (Invitrogen), and place the ZFP constructs under the control of the cytomegalovirus (CMV) promoter. The vector carries ampicillin and neomycin markers for selection in bacteria and mammalian cell culture, respectively. A Kozak sequence for proper translation initiation (Kozak, J. Biol. Chem. 266:19867-19870 (1991)) was incorporated. To achieve

nuclear localization of the products, the nuclear localization sequence (NLS) from the SV40 large T antigen (Pro-Lys-Lys-Lys-Arg-Lys-Val) (Kalderon et al., Cell 39:499-509 (1984)) was added. The insertion site for the ZFP-encoding sequence is followed by the functional domain sequence. The three versions of this vector differ in the functional domain; "pcDNA-NKF" carries the KRAB repression domain sequence, "pcDNA-NVF" carries the VP16 activation domain, and "NF-control" carries no functional domain. Following the functional domain is the FLAG epitope sequence (Kodak) to allow specific detection of the ZFPs.

Detail Description Paragraph:

[0331] The effector plasmid construction is described above. The VEGF1-KRAB, VEGF3a-KRAB, and VEGF3a/1-KRAB expression vectors were designed to produce a fusion of the SV40 nuclear localization sequence, the VEGF ZFP, the KRAB repression domain, and a pcDNA3.1 expression vector was used as a control (pcDNA).

Detail Description Paragraph:

[0337] The effector plasmid construction is described above. The VEGF1-VP16, VEGF3a-VP16, and VEGF3a/1-VP16 expression vectors were designed to produce a fusion of the SV40 nuclear localization sequence, the VEGF ZFP, the VP16 trans-activation domain, and a FLAG epitope tag all under the control of the CMV promoter. The empty pcDNA3 expression vector was used as a control.

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Detail Description Paragraph:

[0253] As another example, vectors for expressing beta protein coding sequence in mammalian cells will include a promoter active in mammalian cells. Such promoters are often drawn from mammalian viruses--such as the enhancer-promoter sequences from the immediate early gene of the human cytomegalovirus (CMV), the enhancer-promoter sequences from the Rous sarcoma virus long terminal repeat (RSV LTR), and the enhancer-promoter from SV40. Often, expression is enhanced by incorporation of polyadenylation sites, such as the late SV40 polyadenylation site and the polyadenylation signal and transcription termination sequences from the bovine growth hormone (BGH) gene, and ribosome binding sites. Furthermore, vectors can include introns, such as intron II of rabbit .beta.-globin gene and the SV40 splice elements.

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bacterial delivery system

L15: Entry 10 of 218

File: PGPB

Oct 6, 2005

DOCUMENT-IDENTIFIER: US 20050222057 A1

TITLE: Intact minicells as vectors for dna transfer and gene therapy in vitro and in vivo

Summary of Invention Paragraph:

[0012] Live attenuated bacterial vectors also are being explored as gene delivery vectors for human gene therapy, including Salmonella (Darji et al., 1997; Paglia et al., 2000; Urashima et al., 2000), Shigella (Sizemore et al., 1995; Grillot-Courvalin et al., 2002), Listeria (Dietrich et al., 1998) and invasive E. coli (Grillot-Courvalin et al., 1998). However, bacterial vectors have significant limitations because live bacteria, though attenuated, must be engineered to carry phagolysosome membrane lysis mechanisms, to enable sufficient recombinant DNA to escape to the mammalian cell cytosol and hence the nucleus. Such engineering is difficult and may be impossible for many intracellular bacterial pathogens. Moreover, mutations that attenuate bacterial pathogens are known for only a few bacterial species, for example mutations in the aromatic amino acid biosynthesis genes for Salmonella, E. coli and Shigella.

Detail Description Paragraph:

[0052] The ability of intact, recombinant minicells of the invention to maintain integrity in vivo makes possible their use in gene therapy, as described above. Intact minicells also carry none of the bacterial genomic DNA that is present in recombinant bacterial cells, for example, of Shigella flexneri, Listeria monocytogenes, Escherichia coli or Salmonella typhimurium, which others have used to transfer eukaryotic expression plasmids into host cells. See Sizemore et al. (1995); Gentshev et al. (2000); Catic et al. (1999); Dietrich et al. (1998); and Courvalin et al. (1995). Accordingly, gene therapy with intact minicells, pursuant to the present invention, does not entail the risk, associated with use of the recombinant bacteria, of the unintended transfer of a bacterial or an antibiotic resistance-marker gene to microbial flora which are indigenous to the patient. Furthermore, recombinant bacteria must be cleared from the patient by means of cell-mediated immunity and, hence, are unsuitable for gene therapy of an immunocompromised patient suffering, for example, from cancer or AIDS.

[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)*intermediate early promoter human cytomeres**vectors donor molecules systems*

Other Reference Publication (86):

Chapman, B.S. et al: "Effect of Intron A from Human Cytomegalovirus (Towne) Immediate-Early Gene on Heterologous Expression in Mammalian Cells". Nucleic Acids Research, BG, Oxford Univrsity Press, Surrey, vol. 19, No. 14, p. 3979-3986.